UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

May 25, 1999

MEMORANDUM:

Subject: EPA Reg. No.:060061-00078/NP-1 ® Plus Sapstain Control Chemical
DP Barcode: D247403
Case No.: 2725
EPA Reg. No.:060061-00027/NP-1 ® Sapstain Control Chemical
DP Barcode: D247400
Case No.: 2725

From: John L. Dupuy Ph.D 5/25/99
Product Reregistration Branch
Special Review and Reregistration Division (7508C) JLD

To: Bonnie Adler, CRM
Product Reregistration Branch
Special Review and Reregistration Division (7508C)

Applicant: Kop-Coat, Inc.
Protection Products Division
5137 Southwest Avenue, St. Louis, MO 63110
314/772-2200

FORMULATION FROM EPA Reg. No.060061-00078 LABEL:

	% by wt.
Active Ingredient(s): Didecyl dimethyl Ammonium Chloride	64.34 %
3-Iodo-2-Propynyl Butyl Carbamate	07.55 %
5-Chloro-2-Methyl-4-Isothiazolin-3-One	00.06 %
2-Methyl-4-Isothiazolin-3-One	00.02 %
Inert Ingredient(s):	28.03 %
Total	100.0%

FORMULATION FROM EPA Reg. No.060061-00027 LABEL:

	% by wt.
Active Ingredient(s): Didecyl dimethyl Ammonium Chloride.....	64.80 %
3-Iodo-2-Propynyl Butyl Carbamate.....	7.60 %
Inert Ingredient(s):.....	27.60 %
Total	100.00%

BACKGROUND: In the 8 month response to the Troysan RED the registrant has submitted acute toxicity studies to support the reregistration of their products, EPA Reg. No. 60061-78 and EPA Reg. No. 60061-27. The MRID's are as follows:CA413944-04, 420538-01, and 411264-01. The studies were conducted by Bushy Run Research Center and Product Investigations. The test material used in the studies was NP-1® Sapstain Control Chemical, a pale yellow, transparent, slightly viscous liquid. The Acute Inhalation Study (81-3) was not submitted for review. Reg. No. 60061-27 and 60061-78 were placed in Batch 4 of the Troysan RED.

RECOMMENDATIONS: With the exception of the skin sensitization the submitted studies are acceptable (81-1, 81-2, 81-4, 81-5) and may be used to support the reregistration of EPA Reg. No.060061-00078 and EPA Reg. No. 060061-00027. The Skin Sensitization Study was not acceptable but was given a Waiver since the Primary Dermal Irritation Testing had a toxicity category of I. The Registrant must cite or submit Acute Inhalation Studies before both Products can be reregistered.

The acute toxicity profile for EPA Reg. No. 60061-27 is currently:

Acute Oral	II	Acceptable
Acute Dermal	III	Acceptable
Acute Inhalation	---	DATA GAP
Primary Eye	I	Acceptable
Primary Dermal	I	Acceptable
Skin Sensitization	non-sensitizer	~~Unacceptable~~ (Waived)

LABELING: This will be done when an acceptable Acute Inhalation study has been received and reviewed.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1, 870.1100)

Product Manager: 31 Velma Noble
MRID No.: CA413944-04

Reviewer: John L. Dupuy Ph. D
Study Completion Date: December 4, 1989
Study No.: 52-642

Testing Facility: Bushy Run Research Center

Author: B.C. Myers & S.M. Christopher

Quality Assurance (40 CFR §160.12): Included

Test Material: NP-1® Plus Sapstain Control Chemical, a pale yellow, transparent, slightly viscous liquid.
Species: Rats; Albino, Sprague-Dawley
Age: Young adult
Weight: Males: 200-250 g; Females:200-250 g

Source: Harlan Sprague-Dawley, Inc.
Conclusion:

1. LD_{50} (mg/kg):
   Males: 331 mg/kg
   Females: 238 mg/kg
   Combined: 262 mg/kg
2. The estimated LD_{50} is 238 mg/kg
3. Tox. Category: II

Classification: Acceptable

Procedure (Deviations from §81-1): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
100	0/5	0/5	0/10
200	0/5	2/5	2/10
283	0/5	N/A	N/A
336	3/5	N/A	N/A
400	5/5	4/5	9/10

Observations: Signs of toxicity included sluggishness, lacrimation, diarrhea and a brown stain on the periurogenital fur, red discharge on the facial fur and emaciation. Deaths occurred at one to 4 days. Survivors recovered at 2 to 5 days.

Gross Necropsy: Necropsy of rats that died revealed discolored lungs (tan to red), discolored

stomachs (yellow red to purple 0, hemorrhaged stomachs, one stomach adhering to liver, red to brown intestines, dark red livers and thoracic cavities filled with red to clear liquid. Two males had blood in the urine. **In survivors, there were no remarkable gross lesions.**

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: 31 Velma Noble
MRID No.: 420538-01

Reviewer: John L. Dupuy Ph. D
Study Completion Date: October 4, 1991
Study No.: 54-588

Testing Facility: Bushy Run Research Center
Author: B.C. Myers & S.M. Christopher

Quality Assurance (40 CFR §160.12): Included

Test Material: NP-1® Sapstain Control Chemical, a pale yellow, transparent, slightly viscous liquid.
Species: Rabbits, New Zealand White
Age: Young adult
Weight: Males: 2.3-2.9 kg; Females: 2.3-2.9 kg

Source: Hazleton Research Products, Inc. (Denver, PA)

Dermal LD_{50} Testing:

Conclusion:

1. LD_{50} (mg/kg):
   Males: 3140 mg/kg
   Females: 2730 mg/kg
   Combined: 2930 mg/kg
2. The estimated LD_{50} is 2730 mg/kg
3. Tox. Category: III

Classification: Acceptable

Procedure (Deviations from §81-2): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
4000	5/5	5/5	10/10
2830	1/5	3/5	4/10
2000	0/5	0/5	0/10

Observations:

Dosage mg/kg	Time of Death	Observations
2000	0/10	Erythema, edema at 1 day; necrosis at 1 to 14 days; ulceration at 14 days.
2830	1/10 at 3 days 2/10 at 4 days 1/10 at 7 days	Erythema at 1 day; edema, necrosis at 1 day to death. Erythema at 1 day; edema, necrosis at 1 day to death. Erythema at 1 day; edema, necrosis at 1 day to death.
4000	4/10 at 3-3.5 hrs. 3/10 at 2 days 2/10 at 3 days 1/10 at 4 days	Erythema, necrosis, ecchymoses at death. Erythema, edema, necrosis at 1 day. Edema at 1 day, necrosis at day 1 to death. Erythema, edema at 1 day; necrosis at1 day to death.

Gross Necropsy:

Dose mg/kg	Gross necropsy observations of animals that died during study
2830	Intestines liquid filled; kidneys enlarged, purple; thymus dark purple, enlarged; lungs dark red; intestines gas-filled; kidneys autolyzed; tissues autolyzed.
4000	Tissues autolyzed; lungs dark red; intestines hemorrhaged.

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: 31 Velma Noble
MRID No.: CA413944-04

Reviewer: John L. Dupuy Ph.D
Study Completion Date: August 31, 1989
Study No.:52-642

Testing Facility: Bushy Run Research Center
Author: B.C. Myers & S.M. Christopher
Quality Assurance (40 CFR §160.12): Included

Test Material: NP-1® Plus Sapstain Control Chemical, a pale yellow, transparent, slightly viscous liquid.
Dosage: 0.1 mL (undiluted)
Species: Rabbits; White New Zealand
Age: Adult
Weight: Male (2.0 to 3 kg.) and Females (2.0 to 3 kg.)

Source: Hazleton-Dutchland , Inc. (Denver, PA).

Conclusion:

1. **Toxicity Category:** I
2. **Classification**: Acceptable

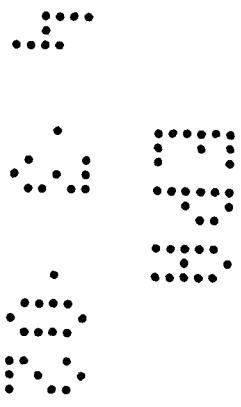
Procedure (Deviations from §81-4): None

Observations	Number "positive"/number tested		
	Hours		
	1	24	48
	Unwashed eyes		
Corneal Opacity	2/2	2/2	2/2
Iritis	0	0	0
Conjunctivae:			
Redness	0	0	0
Chemosis	2/2	2/2	2/2
Discharge	2/2	2/2	2/2

Note: 0= Scoring impossible because of corneal opacity, conjunctival necrosis and/or conjunctival swelling.

Summary: Instillation 0.1 ml of NP-1 Plus (Concentrate) resulted in severe corneal opacity in

both eyes of the male and female dosed within one hour. Because of the severe opacity, it was impossible to score the iris throughout the test. Necrosis of the conjunctivae and nictitating membrane was apparent at one hour prohibiting the scoring of conjunctival redness. Moderate chemosis of the conjunctival was observed in both eyes at one hour developing into severe swelling by 24 hours. Each rabbit also exhibited a purulent ocular discharge at 24 hours. Because of the persistent severe irritation evident at 48 hours, both animals were sacrificed.



DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 31 Velma Noble
MRID No.: CA413944-04

Reviewer: John L. Dupuy Ph..D
Study Completion Date: December 4, 1989
Study No.: 52-642

Testing Facility: Bushy Run Research Center
Author: B.C. Myers & S.M. Christopher

Quality Assurance (40 CFR §160.12): Included

Test Material: NP-1® Plus Sapstain Control Chemical, a pale yellow, transparent, slightly viscous liquid.
Dosage: 0.5 mL
Species: Rabbits; White New Zealand
Age: Adult
Weight: Male (2.0 to 3 kg.) and Females (2.0 to 3 kg.)

Source: Hazleton-Dutchland , Inc. (Denver, PA).

Conclusion:

1. **Toxicity Category:** I
2. **Classification**: Acceptable

Procedure (Deviations from §81-5): None

Results: Application of 0.5 ml of NP-1 Plus (Concentrate) to covered rabbit skin resulted in severe erythema and edema on 2 of 2 rabbits dosed. Poorly defined necrosis was apparent on 2 within one hour following exposure. Both rabbits exhibited severe necrosis an ecchymosis within one day. By 3 days, ulceration was observed on one rabbit. Desquamation and scabs were observed on both animals at 7 days. No erythema or edema persisted at 14 days, but fissuring and alopecia were evident on one of 2 animals and severe necrosis persisted on both rabbits.

Special Comments: None

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: 31 Velma Noble
MRID No.: 411264-01

Reviewer: John L. Dupuy Ph..D
Study Completion Date: May 10, 1989
Study No.: PI-5493

Testing Facility: Product Investigations Inc.
Author: Morris V. Shelanski MD

Quality Assurance (40 CFR §160.12): Included

Test Material: NP-1® Sapstain Control Chemical, a pale yellow, transparent, slightly viscous liquid.
Positive Control Material: none
Species: Homo sapiens
Age: 18 years or older for 51 subjects
Weight: Unknown
Source: Local population
Method: Shelanski and Shelanski Repeated Insult Patch Test

Conclusion:

1. **Dermal Sensitization Study is Unacceptable.** The study has been given a Waiver since the Primary DERMAL IRRITATION IRRITATION TESTING was given a **Toxicity Category:** I which will require PPE.
2. **Classification**: Non Sensitizer

Procedure (Deviations from §81-6): Adult Humans were the test subjects.

Procedure: Not acceptable.

Results: Not acceptable.

ACUTE TOX ONE-LINERS

1. REGISTRATION NO.: 60061-78 and REGISTRATION NO.: 60062-27
2. PC CODE: For REGISTRATION NO.: 60061-78: **069149,107801, 107103, 107102.**
   For REGISTRATION NO.: 60061-27: **069149,107801.**
3. CURRENT DATE: May 19, 1999
4. TEST MATERIAL: NP-1® Plus Sapstain Control Chemical (81-1, 81-4, 81-5)
   NP-1® Sapstain Control Chemical (81-2, 81-6)

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity rat/Bushy Run Research Center, 52-642/12-4-89	CA41394 4-04	Estimated LD50 is 238 mg/kg	II	A
Acute dermal toxicity rabbit/Bushy Run Research Center, 54-588/10-4-91	420538-01	Estimated LD_{50} is 2730 mg/kg	III	A
Acute inhalation toxicity	----------	----------	-----	-------
Primary eye irritation rabbit/Bushy Run Research Center, 52-642/12-4-89	CA41394 4-04	Instillation 0.1 ml of NP-1 Plus (Concentrate) resulted in severe corneal opacity in both eyes of the male and female dosed within one hour. Because of the severe opacity, it was impossible to score the iris throughout the test. Necrosis of the conjunctivae and nictitating membrane was apparent at one hour prohibiting the scoring of conjunctival redness. Moderate chemosis of the conjunctival was observed in both eyes at one hour developing into severe swelling by 24 hours. Each rabbit also exhibited a purulent ocular discharge at 24 hours. Because of the persistent severe irritation evident at 48 hours, both animals were sacrificed.	I	A

Primary dermal irritation rabbit/Bushy Run Research Center, 52-642/12-4-89	CA41394 4-04	Application of 0.5 ml of NP-1 Plus (Concentrate) to covered rabbit skin resulted in severe erythema and edema on 2 of 2 rabbits dosed. Poorly defined necrosis was apparent on 2 within one hour following exposure. Both rabbits exhibited severe necrosis an ecchymosis within one day. By 3 days, ulceration was observed on one rabbit. Desquamation and scabs were observed on both animals at 7 days. No erythema or edema persisted at 14 days, but fissuring and alopecia were evident on one of 2 animals and severe necrosis persisted on both rabbits.	I	A
Dermal sensitization Human Adults/Product Investigations, PI-5493/5-10-89	411264-01	Not a sensitizer	--	U

Core Grade Key: A =Acceptable, S = Supplementary, U = Unacceptable, V = Self Validated